

## Neurocognitive testing (NCT) results following low dose hemi / whole brain irradiation in genetically altered Alzheimer's Dementia (AD) animal models



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### Abstract

**Statement of the Problem:** The use of low dose radiation has been shown to be effective in the resolution of non CNS amyloidosis. Our consortium began looking at various hemi brain and whole brain low dose radiation doses to determine its impact on amyloid and neurocognitive function (NCT).

**Methodology & Theoretical Orientation:** The Detroit group used the APPswePSEN1dE9 murine model, and tested NCT using the Morris Water Maze. The animals received whole brain radiation of 5 x 2 Gy at age 64 week and were tested 5 days before treatment and 8 weeks after treatment. Spatial learning and memory was assessed. The Geneva group used the TgF344-AD rat model. Female animals were treated with 5 x 2 Gy hemi brain irradiation at age 15 months and tested 3 weeks and 3 months after treatment. Open field (locomotor activity) and y maze (working memory) testing were assessed. Control animals were also tested. Animals were sacrificed after testing to determine amyloid-beta plaque changes.

**Findings:** Both models showed a statistically significant improvement in cognitive abilities in the treated animals. Data from Detroit I shown in Fig.1 The treated group displayed significantly reduced latencies ( $31.0 \pm 17.6$  seconds) compared to the untreated group ( $53.9 \pm 14.9$  seconds) across trials on day 5 ( $p = 0.03$ ). These differences were not due to baseline ambulatory /swimming velocities. The Geneva animals showed increased spatial memory index and decreased hyperactivity at 3 months. The test for younger males showed a clear decrease in TSPO in bilateral hippocampi. At sacrifice the Detroit group had noted reduction in amyloid plaque density. The Geneva group could not document a reduction in amyloid density but this may be due to a much higher plaque density in this model.

**Conclusion & Significance:** Based on these results we continue to evaluate the use of different daily / total dose schedules and the use of targeted therapies to determine the role they may play in the treatment of AD.

### Biography

For over three decades, Alvaro Martinez has pioneered several cancer treatments in Radiation Oncology leading to the significant improvement of today's Radiation Therapy outcomes. These include Intensity Modulated Radiation Therapy (IMRT) and Image Guided Radiation Therapy (IGRT) to improve precision and accuracy in radiation treatment delivery, special applicators used to treat prostate, gynecological and other pelvic malignancies to preserve organ function as well as Omnibeam, which is designed for treating very difficult tumors deep within the body. He has published over 360 papers in medical journals and written 54 book chapters. He was an integral part of the conceptual design of the radiation research program into AD and in the development of the clinical trial.



### Publications

1. Marples, B., McGee, M., Callan, B.S., Bowen, S.E. Thibodeau, B.J., Michael, D.B., Maddens, ME., Wilson, G.D., Fontanesi, J and Martinez, A.A. (2015). Low dose cranial irradiation significantly reduces beta amyloid plaques in the brain and improves cognition in a murine model of Alzheimer's Disease (AD) . *Radiother Oncol.* 118: 43-51.
2. Wilson. G.D. and Marples, B. (2016). A new use for an old treatment: Radiation therapy and Alzheimer's disease. *Radiation Research* 185:443-448
3. Kurrus JA, Hayes JK, Hoidal JR, Menendez MM, Elstad MR. (1998). Radiation therapy for tracheobronchial amyloidosis. *Chest.* 114:1489-1492.
4. Poovaneswaran S, Razak AR, Lockman H, Bone M, Pollard K, Mazdai G. (2008).Tracheobronchial amyloidosis: utilization of radiotherapy as a treatment modality. *Medscape Journal of Medicine* 10:42.
5. Neben-Wittich MA, Foote RL, Kalra S. (2007) External beam radiation therapy for tracheobronchial amyloidosis. *Chest* 132:262-267.

[11<sup>th</sup> International Conference on Dementia and Dementia Care](#) | Paris, France | February 19-20, 2020

**Citation:** Alvaro A. Martinez, Neurocognitive testing (NCT) results following low dose hemi / whole brain irradiation in genetically altered Alzheimer's Dementia (AD) animal models, *Dementia Care* 2020: 11th International Conference on Dementia and Dementia Care, Paris, 19-20 February 2020, pp. 05